second oligonucleotide and said third oligonucleotide modification, if present, is different than said second oligonucleotide modification,

an enzyme selected from the group consisting of DNA dependent DNA polymerase and RNA dependent DNA polymerase, and

one or more RNA polymerases that recognize said first and said second oligonucleotide 5' promoter sequences.

142. The kit of claim 141, further comprising a probe able to indicate the presence of said (+) target sequence or said (-) target sequence.

REMARKS

The specification has been amended to indicate that the parent application 08/345,861 has issued as U.S. Patent 5,766,849.

Claims 24-38 and 81 have been canceled. Claims 41, 42, 48, 49, 51, 54-57, 59, 60, 67, 69, 70, 72, 73, 79, 80, 91 and 96 have been amended. New claims 102-142 have been added. Claims 39-42, 48-51, 54-80, and 82-142 are pending in the above captioned application (attached as Appendix A). Applicant submits that the amendment is fully supported by the specification and no new matter is introduced thereby.

Applicant acknowledges that the Examiner has withdrawn rejections under 35 U.S.C. § 103. In addition, Applicant acknowledges Examiner's statements that claims 39-42, 48, 50, 55-56 and 100-101 are free of the prior art, and claims 24-38, 54 and 57-99 are free of the prior art, but are rejected for other reasons.

Double Patenting Rejection

The Examiner rejected claims 24-38 and 54 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 11-12, 15, 17, 20-22, 24, 26 and 29-34 of U.S. Patent 5,554,516. Without agreeing with the Examiner's statement, Applicant submits that claims 24-38 have been canceled and claim 54 has been amended and the obviousness-type double patenting rejection has been rendered moot by the amendment.

Rejections under 35 U.S.C. § 112, 2nd Paragraph

The Examiner rejected claims 24-38, 49, 51, 54 and 56 under 35 U.S.C. § 112, 2nd Paragraph, alleging that it is not clear whether or not there is a second promoter-primer on the same oligonucleotide. Applicant submits that the cancellation of claims 24-38 and the amendment of claims 49, 51, 54 and 56 have rendered this rejection moot.

The Examiner rejected claims 57-73 under 35 U.S.C. § 112, 2nd Paragraph, alleging that improper Markush language is used. Applicant submits that the amendment to claims 57, 59, 60, 67, 69, 70, 72 and 73 has rendered this rejection moot.

The Examiner rejected claims 79-83, 91 and 96-97 under 35 U.S.C. § 112, 2nd Paragraph, and suggested the use of Markush group to clarify the claims. Applicant has amended claims 79, 80, 91 and 96 following the Examiner's suggestion and has canceled claim 81. Therefore, this rejection has also been rendered moot by the amendment.

The Examiner rejected claims 24-38, 49, 51, 54 and 56 under 35 U.S.C. § 112, 2nd Paragraph, alleging that these claims are confusing because of the language "at least two

members" and "in common" therein. Without agreeing with the Examiner's statement, Applicant submits that claims 24-38 have been canceled and claims 49, 51, 54 and 56 have been amended and this rejection under 35 U.S.C. § 112, 2nd Paragraph, has been rendered moot.

Accordingly, Applicant respectfully submits that claims 39-42, 48-51, 54-80, and 82-142 are allowable and a notice to that effect is respectfully requested.

If the fee submitted with this response is incorrect, please charge or credit our Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,

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APPENDIX A: PENDING CLAIMS OF APPLICATION 08/480,472

39. A kit for amplifying *Mycobacterial* nucleic acid, containing at least one of a first and second oligonucleotide; said first oligonucleotide comprising xGCCGTCACCCCACCAACAAGCT (SEQ ID: 1), and said second oligonucleotide comprising xGGGATAAGCCTGGGAAACTGGGTCTAATACC (SEQ ID: 2), wherein x is nothing or is a sequence recognized by an RNA polymerase and each said oligonucleotide is about 22 to about 100 bases in length.

40. An oligonucleotide of about 20 to about 100 bases in length comprising a nucleic acid sequence selected from the group consisting of xGCCGTCACCCCACCAACAAGCT (SEQ ID: 1), xGGGATAAGCCTGGGAAACTGGGTCTAATACC (SEQ ID: 2), xCCAGGCCACTTCCGCTAACC (SEQ ID: 6), xCGCGGAACAGGCTAAACCGCACGC (SEQ ID: 7), and their fully complementary sequences of the same length, wherein x is nothing or is a sequence recognized by an RNA polymerase.

41. A kit for amplifying and detecting *Mycobacterial* nucleic acid, containing a first oligonucleotide of about 24 to about 100 bases in length comprising a nucleotide base sequence GTCTTGTGGTGGAAAGCGCTTTAG (SEQ ID: 3) and one or more of second oligonucleotides of about 23 to about 100 bases in length selected from the group consisting of xGCCGGTCACCCCACCAACAAGCT (SEQ ID: 1) and xGGATAAGCCTGGGAAACTGGGTCTAATACC (SEQ ID: 2), wherein x is nothing or is a sequence recognized by an RNA polymerase.

42. A kit for amplifying and detecting *Mycobacterial* nucleic acid, containing a first oligonucleotide of about 23 to about 100 bases in length comprising a nucleotide base sequence GGAGGATATGTCTCAGCGCTACC (SEQ ID: 8) and one or more of second oligonucleotides

of about 20 to about 100 bases in length selected from the group consisting of xCCAGGCCACTTCCGCTAACC (SEQ ID: 6) and xCGCGGAACAGGCTAAACCGCACGC (SEQ ID: 7), wherein x is nothing or is a sequence recognized by an RNA polymerase.

48. The kit of claim 41, wherein one or more of said second oligonucleotides is modified at 3' end to reduce or block extension of said one or more of said second oligonucleotides by a polymerase.

49. The kit of claim 48, wherein one or more of said second oligonucleotides is unmodified at 3' end.

50. The plurality of oligonucleotides of claim 40, wherein one or more of said oligonucleotides is modified at 3' end to reduce or block extension of said one or more of said oligonucleotides by a polymerase.

51. A plurality of oligonucleotides of claim 40, wherein one or more of said oligonucleotides is unmodified at 3' end and one or more of said oligonucleotides is modified at 3' end to reduce or block extension by a polymerase.

54. The plurality of oligonucleotides of claim 51, wherein one or more of said oligonucleotides is differently modified at 3' end to reduce or block extension by a polymerase.

55. The kit of claim 42, wherein one or more of said second oligonucleotides is modified at 3' end to reduce or block extension of said one or more of said second oligonucleotides by a polymerase.

56. The kit of claim 55, wherein one or more of said second oligonucleotides is

unmodified at 3' end.

57. A nucleic acid hybridization probe, comprising an oligonucleotide from 10 to 100 nucleotides in length which will hybridize with at least 10 contiguous bases of a nucleotide base sequence region of *Mycobacterium tuberculosis* nucleic acid to form a detectable hybridization duplex under selective hybridization conditions, wherein said region consists of a nucleotide base sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 8, and their fully complementary sequences of the same length.

58. The probe of claim 57, wherein said oligonucleotide is from 15 to 50 nucleotides in length.

59. The probe of claim 57, wherein said oligonucleotide comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 8, and their fully complementary sequences of the same length.

60. The probe of claim 57, wherein said oligonucleotide consists of a nucleotide base sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 8, and their fully complementary sequences of the same length.

61. The probe of claim 57 containing a detectable label.

62. The probe of claim 61, wherein said detectable label is an acridinium ester.

63. A specifically detectable nucleic acid hybrid formed under selective hybridization conditions between the hybridization probe of claim 57 and a nucleic acid comprising a *Mycobacterium tuberculosis* nucleotide base sequence.

64. A specifically detectable nucleic acid hybrid formed under selective hybridization conditions between the hybridization probe of claim 58 and a nucleic acid comprising a *Mycobacterium tuberculosis* nucleotide base sequence.

65. A specifically detectable nucleic acid hybrid formed under selective hybridization conditions between the hybridization probe of claim 59 and a nucleic acid comprising a *Mycobacterium tuberculosis* nucleotide base sequence.

66. A specifically detectable nucleic acid hybrid formed under selective hybridization conditions between the hybridization probe of claim 60 and a nucleic acid comprising a *Mycobacterium tuberculosis* nucleotide base sequence.

67. An oligonucleotide from 10 to 100 nucleotides in length able to bind to or extend through a region of *Mycobacterium tuberculosis* nucleic acid, wherein said region consists of a nucleotide base sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 7, SEQ ID NO: 22 and SEQ ID NO: 23, and their fully complementary sequences of the same length.

68. The oligonucleotide of claim 67 from 15 to 50 nucleotides in length.

69. The oligonucleotide of claim 67, comprising a nucleotide base sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 7, SEQ ID NO: 22 and SEQ ID NO: 23, and their fully complementary sequences of the same length.

70. The oligonucleotide of claim 67, consisting of a nucleotide base sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 7, SEQ ID NO: 22 and SEQ ID NO: 23, and their fully complementary sequences of the same length.

71. The oligonucleotide of claim 67 which comprises, in the 5' upstream region, an oligonucleotide sequence which is recognizable by an RNA polymerase and enhances initiation or elongation by said RNA polymerase.

72. The oligonucleotide of claim 71, comprising a nucleotide base sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 6 and SEQ ID NO: 19.

73. The oligonucleotide of claim 71, consisting of a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 6 and SEQ ID NO: 19.

74. A composition able to amplify *Mycobacterium tuberculosis* nucleic acid, comprising: one or more oligonucleotide from about 10 to about 100 nucleotide bases in length which will, under nucleic acid amplification conditions, bind to or extend through a region of *Mycobacterium tuberculosis* nucleic acid consisting of a nucleotide base sequence, said region selected from the group consisting of:

a) SEQ ID NO: 23,

b) SEQ ID NO: 8,

c) SEQ ID NO: 7,

d) SEQ ID NO: 9,

e) SEQ ID NO: 10, and

f) the nucleotide sequences perfectly complementary to these sequences.

75. The composition of claim 74 comprising two or more said oligonucleotides.

76. The composition of claim 74 comprising a first oligonucleotide which comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 23, and SEQ ID NO: 7.

77. The composition of claim 76 comprising a second oligonucleotide which comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 23, and SEQ ID NO: 7.

78. The composition of any one of claims 74, 75, or 76, wherein one or more oligonucleotide further comprises, in the 5' upstream region, a nucleotide base sequence which is recognized by an RNA polymerase and which enhances transcription initiation or polymerization by said RNA polymerase.

79. The composition of any one of claims 74, 76, or 77, further comprising a nucleic acid hybridization assay probe from about 10 to about 100 nucleotide bases in length which will hybridize with at least 10 contiguous bases of a nucleotide base sequence region of *Mycobacterium tuberculosis* nucleic acid to form a detectable duplex under hybridization conditions; wherein said region is selected from the group consisting of SEQ ID NO: 8 and the perfectly complementary sequence thereto.

80. The composition of claim 79, wherein said probe comprises an oligonucleotide selected from the group consisting of SEQ ID NO: 8 and the perfectly complementary sequence thereto.

82. The composition of claim 79 wherein said probe contains a detectable label.

83. The composition of claim 82 wherein said detectable label is an acridinium ester.

84. A composition able to amplify *Mycobacterium tuberculosis* nucleic acid, comprising: one or more oligonucleotide from about 10 to about 100 nucleotide bases in length which will, under nucleic acid amplification conditions, bind to or extend through a region of *Mycobacterium tuberculosis* nucleic acid consisting of a nucleotide base sequence, said region selected from the group consisting of:

a) SEQ ID NO: 22,

b) SEQ ID NO: 3,

c) SEQ ID NO: 2,

d) SEQ ID NO: 4,

e) SEQ ID NO: 5, and

f) the nucleotide sequences perfectly complementary to these sequences.

85. The composition of claim 84 comprising two or more said oligonucleotides.

86. The composition of claim 84 comprising a first oligonucleotide which comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 22, and SEQ ID NO: 2.

87. The composition of claim 86 comprising a second oligonucleotide which comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 22, and SEQ ID NO: 2.

88. The composition of any one of claims 84, 85, or 86, wherein one or more oligonucleotide further comprises, in the 5' upstream region, a nucleotide base sequence which is

recognized by an RNA polymerase and which enhances transcription initiation or polymerization by said RNA polymerase.

89. The composition of any one of claims 84, 86, or 87, further comprising a nucleic acid hybridization assay probe from about 10 to about 100 nucleotide bases in length which will hybridize with at least 10 contiguous bases of a nucleotide base sequence region of *Mycobacterium tuberculosis* nucleic acid to form a detectable duplex under hybridization conditions; said region consisting of SEQ ID NO: 3 or the perfectly complementary sequence thereto.

90. The composition of claim 89, wherein said probe comprises an oligonucleotide with a nucleotide base sequence comprising SEQ ID NO: 3 or the perfectly complementary sequence thereto.

91. The composition of claim 89, wherein said probe comprises an oligonucleotide selected from the group consisting of SEQ ID NO: 3 and the perfectly complementary sequence thereto.

92. The composition of claim 84 wherein said probe contains a detectable label.

93. The composition of claim 92 wherein said detectable label is an acridinium ester.

94. A helper probe consisting essentially of a nucleotide sequence selected from the group consisting of: SEQ ID NO:9, and SEQ ID NO:10.

95. A helper probe consisting essentially of a nucleotide sequence selected from the group consisting of: SEQ ID NO:4, and SEQ ID NO:5.

96. A probe mix comprising:

a nucleic acid hybridization assay probe comprising an oligonucleotide from 10 to 100 nucleotides in length which will hybridize with at least 10 contiguous bases of a region of *Mycobacterium tuberculosis* nucleic acid to form a detectable hybridization duplex under selective hybridization conditions, wherein said region is selected from the group consisting of SEQ ID NO. 8 and its fully complementary sequence of the same length, and a helper probe.

97. The probe mix of claim 96, wherein said helper probe consists essentially of a nucleic acid sequence selected from the group consisting of: SEQ ID NO:9, and SEQ ID NO:10.

98. A probe mix comprising:

a nucleic acid hybridization assay probe comprising an oligonucleotide from 10 to 100 nucleotides in length which will hybridize with at least 10 contiguous bases of a region of *Mycobacterium tuberculosis* nucleic acid to form a detectable hybridization duplex under selective hybridization conditions, wherein said region consists of SEQ ID NO. 3, or its fully complementary sequence of the same length, and

a helper probe.

99. The probe mix of claim 98, wherein said helper probe consists essentially of a nucleic acid sequence selected from the group consisting of: SEQ ID NO:4, and SEQ ID NO:5.

100. A kit for amplifying *Mycobacterial* nucleic acid, containing a first oligonucleotide comprising xCCAGGCCACTTCCGCTAACC (SEQ ID: 6), and a second oligonucleotide comprising x'CGCGGAACAGGCTAAACCGCACGC (SEQ ID: 7), wherein x is nothing or is a

sequence recognized by an RNA polymerase and x' is nothing or is a sequence recognized by an RNA polymerase.

101. A composition useful in the detection of *Mycobacterium tuberculosis* comprising at least one oligonucleotide, or composition containing an oligonucleotide, selected from the group consisting of:

a) a nucleic acid hybridization assay probe from about 10 to about 100 nucleotide bases in length comprising an oligonucleotide which will hybridize to at least 10 contiguous bases of a nucleotide base sequence region of a target *Mycobacterium tuberculosis* nucleic acid, said region selected from the group consisting SEQ ID NO: 3, SEQ ID NO: 8, and the sequences perfectly complementary thereto;

b) an oligonucleotide from about 10 to about 100 nucleotide bases in length able to bind to or extend through a region of *Mycobacterium tuberculosis* nucleic acid, said region consisting of a nucleotide base sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 22, SEQ ID NO: 23, and the sequences perfectly complementary to these sequences,

c) a kit comprising the oligonucleotide of b), and

d) a specifically detectable nucleic acid hybrid formed under nucleic acid hybridization conditions between the hybridization assay probe of a) and a nucleic acid comprising a *Mycobacterium tuberculosis* nucleotide base sequence.

102. A composition comprising:

a nucleic acid comprising a (+) target sequence,

a first oligonucleotide comprising a primer sequence able to hybridize at or near the 3'-end of said (+) target sequence, a 5' promoter sequence, and a modification at or near the 3' end of said first oligonucleotide primer sequence which reduces or blocks extension of said first

oligonucleotide primer sequence by a polymerase compared to said first oligonucleotide primer sequence not having said modification,

a second oligonucleotide comprising a primer sequence able to hybridize at or near said 3'-end of said (+) target sequence, a 5' promoter sequence, and an optionally present modification at or near the 3' end of said second oligonucleotide primer sequence which reduces or blocks extension of said second oligonucleotide primer sequence by a polymerase compared to said second oligonucleotide primer sequence not having said modification, wherein said second oligonucleotide hybridizes to said (+) target sequence in effectively the same position as said first oligonucleotide and said second oligonucleotide modification, if present, is different than said first oligonucleotide modification,

a third oligonucleotide comprising a primer sequence able to hybridize to the 3'-end of a (-) target nucleic acid sequence which is produced during said method and which is the complement of said (+) target sequence, an optionally present 5' promoter sequence, and an optionally present modification at or near the 3' end of said third oligonucleotide primer sequence able to reduce or block extension of said third oligonucleotide primer sequence by a polymerase compared to said third oligonucleotide primer sequence not having said modification,

an enzyme selected from the group consisting of DNA dependent DNA polymerase and RNA dependent DNA polymerase, and

one or more RNA polymerases that recognize said first and said second oligonucleotide 5' promoter sequences.

103. The composition of claim 102, wherein said (+) target sequence is RNA.

104. The composition of claim 102, wherein said composition further comprises RNAse H activity.

105. The composition of claim 104, wherein said RNAse H activity is supplied by an exogenous RNAse H from *E. coli*.

106. The composition of claim 104, wherein said RNAse H activity is supplied by a reverse transcriptase.

107. The composition of claim 102, wherein said enzyme is a reverse transcriptase which is both a DNA-dependent DNA polymerase and an RNA-dependent DNA polymerase.

108. The composition of claim 102, further comprising a molecule selected from the group consisting of DMSO, dimethylformamide, ethylene glycol, zinc and glycerol.

109. The composition of claim 102, further comprising a helper oligonucleotide.

110. The composition of claim 102, wherein said first and said second oligonucleotides are present in a molar ratio of between 1:1 and 1000:1.

111. The composition of claim 102, wherein said second oligonucleotide contains said modification.

112. The composition of claim 111, further comprising a fourth oligonucleotide comprising a primer sequence that hybridizes in effectively the same position as said first and second oligonucleotides and an optionally present 5' promoter sequence, wherein said fourth oligonucleotide does not contain a modification at or near its 3' end to reduce or block primer extension of said fourth oligonucleotide primer sequence.

113. The composition of claim 102, wherein said first oligonucleotide modification and

said second oligonucleotide modification are each independently selected from the group consisting of alkane diol modification, 3' deoxynucleotide residue, nucleotide with a nonphosphodiester linkage, non-nucleotide modification, base non-complementary to said (+) target sequence, and dideoxynucleotide.

114. The composition of claim 102, wherein said first oligonucleotide modification and said second oligonucleotide modification are each independently selected from the group consisting of cordycepin, ribonucleotide, and phosphorothioate nucleotide.

115. The composition of claim 102, wherein said third oligonucleotide does not contain said modification.

116. The composition of claim 102, wherein said third oligonucleotide contains said 5' promoter sequence.

117. The composition of claim 116, wherein said third oligonucleotide contains said modification.

118. The composition of claim 102, wherein said first and said second oligonucleotide primer sequences are the same.

119. The composition of claim 102, wherein said first and said second oligonucleotide primer sequences are different.

120. A composition comprising:

a nucleic acid comprising a (+) target sequence,

a first oligonucleotide comprising a primer sequence able to hybridize to the 3'-

end of said (+) target sequence, an optionally present 5' promoter sequence, and an optionally present modification at or near the 3' end of said first oligonucleotide primer sequence able to reduce or block extension of said first oligonucleotide primer sequence by a polymerase compared to said first oligonucleotide primer sequence not having said modification,

a second oligonucleotide comprising a primer sequence able to hybridize at or near the 3'-end of a (-) target nucleic acid sequence which is produced during said method and which is the complement of said (+) target sequence, a 5' promoter sequence, and a modification at or near the 3' end of said second oligonucleotide primer sequence which reduces or blocks extension of said second oligonucleotide primer sequence by a polymerase compared to said second oligonucleotide primer sequence not having said modification,

a third oligonucleotide comprising a primer sequence able to hybridize at or near said 3'-end of said (-) target sequence, a 5' promoter sequence, and an optionally present modification at or near the 3' end of said third oligonucleotide primer sequence which reduces or blocks extension of said third oligonucleotide primer sequence by a polymerase compared to said third oligonucleotide primer sequence not having said modification, wherein said third oligonucleotide hybridizes to said (-) target sequence in effectively the same position as said second oligonucleotide and said third oligonucleotide modification, if present, is different than said second oligonucleotide modification,

an enzyme selected from the group consisting of DNA dependent DNA polymerase and RNA dependent DNA polymerase, and

one or more RNA polymerases that recognize said first and said second oligonucleotide 5' promoter sequences.

121. The composition of claim 120, wherein said (+) target sequence is RNA.

122. The composition of claim 120, wherein said composition further comprises RNAse H activity.

123. The composition of claim 122, wherein said RNAse H activity is supplied by an exogenous RNAse H from *E. coli*.

124. The composition of claim 122, wherein said RNAse H activity is supplied by a reverse transcriptase.

125. The composition of claim 120, wherein said enzyme is a reverse transcriptase which is both a DNA-dependent DNA polymerase and an RNA-dependent DNA polymerase.

126. The composition of claim 120, further comprising a molecule selected from the group consisting of DMSO, dimethylformamide, ethylene glycol, zinc and glycerol.

127. The composition of claim 120, further comprising a helper oligonucleotide.

128. The composition of claim 120, wherein said second and said third oligonucleotides are present in a molar ratio of between 1:1 and 1000:1.

129. The composition of claim 120, wherein said third oligonucleotide contains said modification.

130. The composition of claim 129, further comprising a fourth oligonucleotide comprising a primer sequence that hybridizes in effectively the same position as said second and third oligonucleotides and an optionally present 5' promoter sequence, wherein said fourth oligonucleotide does not contain a modification at or near its 3' end to reduce or block primer extension of said fourth oligonucleotide primer sequence.

131. The composition of claim 120, wherein said second oligonucleotide modification and said third oligonucleotide modification are each independently selected from the group consisting of alkane diol modification, 3' deoxynucleotide residue, nucleotide with a nonphosphodiester linkage, non-nucleotide modification, base non-complementary to said (+) target sequence, and dideoxynucleotide.

132. The composition of claim 120, wherein said first oligonucleotide modification and said second oligonucleotide modification are each independently selected from the group consisting of cordycepin, ribonucleotide, and phosphorothioate nucleotide.

133. The composition of claim 120, wherein said first oligonucleotide does not contain said modification.

134. The composition of claim 120, wherein said first oligonucleotide contains said 5' promoter sequence.

135. The composition of claim 120, wherein said third oligonucleotide contains said modification.

136. The composition of claim 134, wherein said first oligonucleotide 5' promoter sequence, said second oligonucleotide 5' promoter sequence and said third oligonucleotide 5' promoter sequence are the same.

137. The composition of claim 120, wherein said second and said third oligonucleotide primer sequences are the same.

138. The composition of claim 120, wherein said second and said third oligonucleotide

primer sequences are different.

139. A kit comprising:

a first oligonucleotide comprising a primer sequence able to hybridize at or near the 3'-end of a (+) target sequence, a 5' promoter sequence, and a modification at or near the 3' end of said first oligonucleotide primer sequence which reduces or blocks extension of said first oligonucleotide primer sequence by a polymerase compared to said first oligonucleotide primer sequence not having said modification,

a second oligonucleotide comprising a primer sequence able to hybridize at or near said 3'-end of said (+) target sequence, a 5' promoter sequence, and an optionally present modification at or near the 3' end of said second oligonucleotide primer sequence which reduces or blocks extension of said second oligonucleotide primer sequence by a polymerase compared to said second oligonucleotide primer sequence not having said modification, wherein said second oligonucleotide hybridizes to said (+) target sequence in effectively the same position as said first oligonucleotide and said second oligonucleotide modification, if present, is different than said first oligonucleotide modification,

a third oligonucleotide comprising a primer sequence able to hybridize to the 3'-end of a (-) target nucleic acid sequence which is produced during said method and which is the complement of said (+) target sequence, an optionally present 5' promoter sequence, and an optionally present modification at or near the 3' end of said third oligonucleotide primer sequence able to reduce or block extension of said third oligonucleotide primer sequence by a polymerase compared to said third oligonucleotide primer sequence not having said modification,

an enzyme selected from the group consisting of DNA dependent DNA polymerase and RNA dependent DNA polymerase, and

one or more RNA polymerases that recognize said first and said second oligonucleotide 5' promoter sequences.

140. The kit of claim 139, further comprising a probe able to indicate the presence of said (+) target sequence or said (-) target sequence.

141. A kit comprising:

a first oligonucleotide comprising a primer sequence able to hybridize to the 3'-end of a (+) target sequence, an optionally present 5' promoter sequence, and an optionally present modification at or near the 3' end of said first oligonucleotide primer sequence able to reduce or block extension of said first oligonucleotide primer sequence by a polymerase compared to said first oligonucleotide primer sequence not having said modification,

a second oligonucleotide comprising a primer sequence able to hybridize at or near the 3'-end of a (-) target nucleic acid sequence which is produced during said method and which is the complement of said (+) target sequence, a 5' promoter sequence, and a modification at or near the 3' end of said second oligonucleotide primer sequence which reduces or blocks extension of said second oligonucleotide primer sequence by a polymerase compared to said second oligonucleotide primer sequence not having said modification,

a third oligonucleotide comprising a primer sequence able to hybridize at or near said 3'-end of said (-) target sequence, a 5' promoter sequence, and an optionally present modification at or near the 3' end of said third oligonucleotide primer sequence which reduces or blocks extension of said third oligonucleotide primer sequence by a polymerase compared to said third oligonucleotide primer sequence not having said modification, wherein said third oligonucleotide hybridizes to said (-) target sequence in effectively the same position as said second oligonucleotide and said third oligonucleotide modification, if present, is different than said second oligonucleotide modification,

an enzyme selected from the group consisting of DNA dependent DNA polymerase and RNA dependent DNA polymerase, and

one or more RNA polymerases that recognize said first and said second oligonucleotide 5'

promoter sequences.

142. The kit of claim 141, further comprising a probe able to indicate the presence of said (+) target sequence or said (-) target sequence.